BC Cancer Protocol Summary for Therapy for Non-Metastatic Castration Resistant Prostate Cancer Using Enzalutamide

Protocol Code: *UGUNMPENZ*

Tumour Group: *Genitourinary*

Contact Physician: *Dr. Christian Kollmannsberger*

ELIGIBILITY:

- ECOG performance status 0-2
- Patients with non-metastatic castration resistant prostate cancer (nmCRPC) who are chemotherapy naïve
- Patients with nmCRPC with a PSA doubling time of less or equal to 10 months.
- Patients with no radiologic evidence of metastases (negative bone scan, negative CT of pelvis, abdomen, chest)
- Patients with nmCRPC can receive either apalutamide (UGUPAPA) OR enzalutamide (UGUNMPENZ) but not their sequential use
- Patients who have progressed on enzalutamide in nmCRPC (UGUNMPENZ)
  - Are eligible to receive DOCEtaxel (GUPDOC) and/or cabazitaxel in metastatic CRPC
  - Are **NOT** eligible to receive enzalutamide (UGUPENZ) or abiraterone (UGUPABI) in metastatic CRPC
- A BC Cancer "Compassionate Access Program" (CAP) request must be approved prior to treatment

EXCLUSIONS:

- Metastatic prostate cancer
- Prior treatment with apalutamide in nmCRPC
- Prior treatment with docetaxel plus androgen deprivation therapy (GUPDOCADT)
- Uncontrolled hypertension (systolic blood pressure greater than 160 mmHg or diastolic greater than 95 mmHg)

TESTS:

- Baseline: CBC and differential, platelets, creatinine, sodium, potassium, blood pressure
- Patients at risk for electrolyte abnormality and QTc prolongation: ECG
- Each time seen by physician: PSA, blood pressure.
- If clinically indicated: creatinine, sodium, potassium, ECG

TREATMENT

Drug	Dose	BCCA Administration Guideline
enzalutamide	160 mg daily	PO

One cycle consists of 4 weeks (30 days) of enzalutamide. Dispense 30 day supply. Treat until disease progression or unacceptable toxicity.

Warning: The information contained in these documents are a statement of consensus of BC Cancer professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is at your own risk and is subject to BC Cancer's terms of use available at www.bccancer.bc.ca/terms-of-use

Dose reduction:
Dose level -1: enzalutamide120 mg PO daily
Dose level -2: enzalutamide 80 mg PO daily

Androgen ablative therapy (e.g., LHRH agonist, LHRH antagonist) should be maintained. Discontinue other antiandrogen (e.g., bicalutamide), if used as part of combined androgen blockade.

PRECAUTIONS:

1. **QT prolongation:** Enzalutamide is associated with QTc prolongation. It should be used with caution in patients with a known history of QT prolongation, risk factors for torsade de pointes (e.g. hypokalemia) or patients who are taking medications known to prolong the QT interval.
2. **Seizure:** Enzalutamide is associated with an increased risk of seizure, with a greater risk of seizure at daily doses higher than 160 mg. Seizures resolved after treatment cessation.
3. **Hypertension:** Enzalutamide is associated with increased blood pressure in approximately 7% of patients. Hypertension rarely leads to discontinuation or dose modification, but may require antihypertensive treatment. Blood pressure will need to be monitored once every 2 weeks for the first three months of enzalutamide therapy. Temporary suspension of enzalutamide is recommended for patients with severe hypertension (greater than 200 mmHg systolic or greater than 110 mmHg diastolic). Treatment with enzalutamide may be resumed once hypertension is controlled.
4. **Drug interactions**: CYP2C8 inhibitors (e.g. gemfibrozil) may increase the serum level of enzalutamide. Consider reducing enzalutamide to 120 mg or 80 mg once daily in patients who must be co-administered with a strong CYP2C8 inhibitor.

Call Dr. Christian Kollmannsberger or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Sternberg CN, Fizazi K, Saad F, et at. Enzalutamide and Survival in Nonmetastatic Castration-Resistant Prostate Cancer. N Engl J Med. 2020;382:2197-206
2. Hussain M, Fizazi K, Saad F, et al. Enzalutamide in Men with Nonmetastatic, Castration-Resistant Prostate Cancer. N Engl J Med. 2018; 378:2465-74

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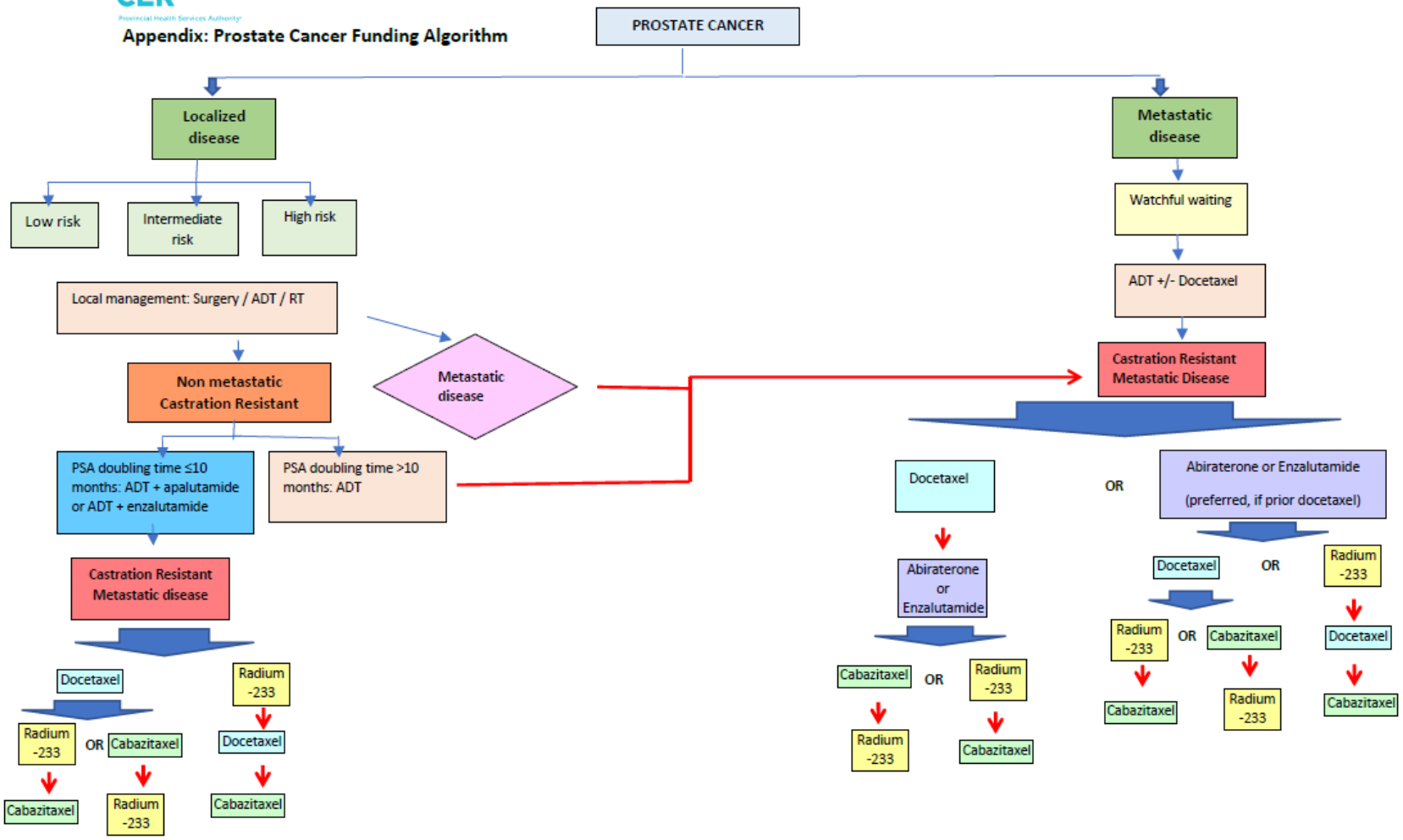
Appendix: Prostate Cancer Funding Algorithm



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